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10/510,937	02/03/2006	Chul-Woo Kim	HANOL-09641	7099

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EXAMINER	
RIGGS II, LARRY D	

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1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,937	KIM ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,15 and 17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,15 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04 August 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 11 August 2009 are acknowledged and entered.

Status of Claims

Claims 1-11, 13, 14, 16, 21 and 22 are cancelled. Claims 12, 15 and 17-20 are currently pending and under consideration.

Withdrawn Rejections/Objections

The rejection of claims 1-20 under 35 U.S.C. §112, First Paragraph, in the Office action mailed 11 May 2009 is withdrawn in view of the amendments filed 11 August 2009.

The rejection of claims 1-20 under 35 U.S.C. §112, Second Paragraph, in the Office action mailed 11 May 2009 is withdrawn in view of the amendments filed 11 August 2009.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 15 and 17-20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites "the proteome standard is one or more proteins selected from the group consisting of the spots in table 1; and diagnosing said subject with breast cancer when said proteome is indicative of said subject having breast cancer". The metes and bounds of the limitation are unclear because table 1 (specification, page 18) only recites number identifiers, molecular weights and isoelectric points. One skilled in the art would be uncertain what proteins correspond with the number identifiers, molecular weights and isoelectric points. Likewise, one skilled in the art would be uncertain how to diagnosis a patient as having breast cancer from a two-dimensional image "serum proteome pattern" when there is no information what proteins the "spots" of table 1 are and there does not seem to be a "proteome pattern" in Table 1 from which to compare.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyagi et al. (US 4,338,811) in view of Sidransky (Nature Reviews, 2002, 2, 210-219), as supported by Romero et al., (Eur. Respir. J., 1996, 9, 17-23).

The instant claims provide a method of diagnosing breast cancer using a proteome image mining tool comprising creating a database of proteome standard from optimal features of into 2D images from the serum proteome of

normal and individuals with breast cancer, extracting features from the 2D image of the serum proteome of a subject of interest, and comparing the subject's proteome pattern to the proteome standard pattern for breast cancer diagnosis, wherein the proteome standard is one or more proteins selected from the spots of table 1.

In light of the indefiniteness of the identification of spots and lack of proteome standard pattern in table 1, the limitation "wherein the proteome standard is one or more proteins selected from the spots of table 1" will be interpreted to comprise any known breast cancer marker which has a molecular weight as set forth in Table 1.

Regarding claim 12 and 18, Miyagi et al. shows a disease diagnostic method in which a 2D pattern diagram representing substances in a body fluid of a subject, is compared for disease diagnostic purposes with a 2D pattern diagram that met particular thresholds (optimal features), stored in a file, representing substances from normal and abnormal patients classified by diseases, (abstract; column 2, line 52 – column 3, line 49).

Miyagi et al. does not show serum features associated with breast cancer.

Sidransky shows proteins that are known markers from patient serum associated with breast cancer, ERBB2 (HER2/neu), CA15-3 (MS1), CEAsd, CA125, (page 210, right column; page 215, right column; Table 1; Figure 2).

For information purposes, Romero et al., (Eur. Respir. J., 1996, 9, 17-23), shows molecular weights of common serum markers associated with cancer, CA15-3, 290 KDa; CEA, 200 KDa; CYFRA 21-1, 40 KDa, (page 22, right column,

first paragraph), thereby supporting that the cancer markers of Sidransky have molecular weights as disclosed in instant Table 1.

Regarding claim 18, Miyagi et al. shows a database of pattern diagram data of the subject and analysis results recorded, (Figure 4).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of disease diagnosis of Miyagi et al. with the serum proteomic data related to breast cancer by Sidransky because a proteome pattern comparison is a useful diagnostic tool for identifying cancer in a patient (Sidransky, Figure 2).

Claim 12, 15, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyagi et al. (US 4,338,811) in view of Sidransky (Nature Reviews, 2002, 2, 210-219) as supported by Romero et al., (Eur. Respir. J., 1996, 9, 17-23) as applied to claims 12 and 18 above, and further in view of Srinivas et al. (Clinical Chemistry, 2001, 47(10), 1901-1911).

The instant claim 15 and 17 depend from claim 12 with the extra limitations that for step 1) extracting correlations between spots utilizes experimental knowledge and a statistical method, and classifying the extracted correlations utilizes a statistical method (claim 15); and for step 3) pattern matching of the subject utilizes features, estimation functions and a fine classification step (claims 17).

Miyagi et al. and Sidransky are applied to claims 12 and 18 above.

Regarding claims 15 and 17, Miyagi et al. shows peak areas of substances are integrated with respect to a preset slope reference, (Figure 2A) and retention times of peaks is subject to variation (experimental variation), where the 2D pattern diagram shows the relation between peak retention times and levels to be used for the disease diagnosis, (column 3, line 1 – column 4, line 14). Miyagi et al. shows that in the course of creating a pattern diagram, a correlation coefficient taking into account the importance of each individual peak or substance in relation to the diagnosis may be used to modify the peak level or area, in the process of disease diagnosis by comparison of the pattern diagrams (column 3, second paragraph; column 4, lines 57-62), meeting the limitations of correlation by experimental knowledge and pattern matching by features and estimation functions.

Miyagi et al. and Sidransky do not show correlating and classifying by a statistical method; nor a fine classification step.

Srivinas et al. shows software packages and bioinformatics tools to analyze two-dimensional gel electrophoresis (2DE) protein patterns, including tools that help in segmentation and detection of protein spots on the images, matching and edition; additional features include pattern recognitions capabilities and the ability to perform multivariate statistics, (page 1907, left column, second paragraph; Figure 4). Srivinas et al. shows protein data derived from 2DE analysis has been used to develop artificial learning models to help classify tumors into benign, borderline, and malignant; and statistical algorithms such as

partial least squares and hierarchical clustering have been used to that effect, (page 1907, right column, second to last paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of disease diagnosis of Miyagi et al. in view of Sidransky with the statistical clustering and pattern matching by Srinivas et al. because by Sidransky shows that bioinformatic tools are needed at all levels of proteomic analysis (page 1906, right column, last paragraph) and Srinivas et al. shows that automated techniques in clustering and pattern matching substantially reduce the amount of knowledge required by users and proteomics is essential in determining those changes in protein profiles that can lead to a more comprehensive understanding of the disease process, (page 1907, right column, first paragraph; page 1908, right column, first paragraph).

Claims 12 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyagi et al. (US 4,338,811) in view of Sidransky (Nature Reviews, 2002, 2, 210-219), as supported by Romero et al., (Eur. Respir. J., 1996, 9, 17-23) as applied to claims 12 and 18 above, in view of Vachtesvanos et al. (US 6,650,779) and further in view of Karlsen et al. (Opt. Eng., 2000, 39(3), 704-711).

The instant claim 19 depends from claim 12 with the extra limitations for step 1) comprises a pre-processing step of performing noise filtering, image enhancement, ortho-projection and edge detection, a feature extraction step producing labeled features, and an evolutionary classification step with a genetic

algorithm discriminating optimal features, estimating fidelity of the optimal feature data discriminated with a support vector machine (SVM) using estimation functions and classification error rates (claim 19);

The instant claim 20 depends from claim 12 with the extra limitations for step 1) comprises a fuzzy data mapping step of computing correlations between spots from the pre-processing step, classifying the computed features by a statistical method, quantifying statistical inaccuracy using a fuzzy technique, and a rule-based classification step of arranging and normalizing the results obtained at the data mapping step resulting in a final rule base (claim 20).

Miyagi et al. and Sidransky are applied to claims 12 and 18 above. Miyagi et al. and Sidransky do not show the image pre-processing step and classification step with a genetic algorithm or the fidelity estimation using a SVM of claim 19. Likewise, Miyagi et al. and Sidransky do not show fuzzy data mapping, quantifying statistical inaccuracy using a fuzzy technique and a rule-based classification step of claim 20.

Regarding claims 19 and 20, Vachtesvanos et al. shows pre-processing a digitized 2D image including edge detection enhancement, de-noising, and projection onto an orthonormal basis function, (column 8, lines 10-43; column 24, lines 3-50) and labeling extracted features, (column 10, lines 1-18). Vachtesvanos et al. shows a genetic algorithm employed to train a wavelet neural network for classification, (column 22, lines 1-10). Vachtesvanos et al. shows estimation functions and classification error rates, (column 21, lines 18 – column 22, line 10). Vachtesvanos et al. shows mapping from a feature space to

a decision space, where detection and classification can occur by fuzzy logic, e.g. fuzzy C-Means, fuzzy relational matrix, fuzzy rule-base classification, etc., (column 3, line 35 - column 4, line 23). Vachtesvanos et al. shows that fuzzy C-means can assign a degree of association of a feature with a partition, (quantifying a statistical inaccuracy of a classification), (column 4, lines 50-65).

Miyagi et al., Sidransky and Vachtesvanos et al. do not show a SVM.

Karleen et al. shows a SVM algorithm classifier of features from images compared to classification by a plurality of neural networks, using estimation functions and classification error rates, (abstract, page 704, right column, second paragraph; page 706, left column; page 708; page 709, right column; Figure 6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of disease diagnosis of Miyagi et al. in view of Sidransky with the image pre-processing and feature classification by Vachtesvanos et al. and the classification SVM algorithm by Karlsen et al. because Vachtesvanos et al. shows that image pre-processing enhances the real signal and improves the quality of feature extraction while the multidimensional neural network analyzes and identifies patterns efficiently and economically while lessening the need for human assistance (column 12, lines 57-61; abstract) and Karlsen et al. shows that the SVM algorithm gives higher correct classification results compared to neural networks, (abstract).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/
Larry Riggs
Examiner, Art Unit 1631

/Marjorie Moran/
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